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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,863	01/15/2004	Leonard Presta	P1726R1D1	5958

9157 7590 10/11/2005

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/757,863	PRESTA, LEONARD	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

1. Applicant's species election of IgG1 and position 298 without traverse, filed 08/19/2005, is acknowledged. It is noted that claims readable on the elected species are claims 1-11, and 14. Claims 12 and 13 do not read one the elected species.

Claims 1-14 are pending.

Claims 12 and 13 are withdrawn from further consideration by the Examnier, 37 C.F.R. 1.142(b) as drawn to non-elected species.

Claims 1-11, and 14 are under consideration.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 8-11, and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No: 6,528,624 (claims priority of provisional application No: 60/080,477, filed 04/02/1998, Reference No 16 cited in IDS).

The '624 Patent teaches a method of making and using of a polypeptide variant comprising a human IgG Fc region comprising amino acid substitution at positions including 333 or 334 (see Table 3 and column 42, in particular). The '642 Patent further teaches that the variant polypeptides can be used in treating a mammal comprising administering a therapeutically effective amount of the variants (see lines 37-41 of column 5).

Therefore, the reference teachings anticipate the claimed invention.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-11, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-11 and 14 encompass a method of treating a disorder in a mammal comprising administering therapeutically effective amount of an Fc-bearing peptide with altered amino acids in the Fc region and enhanced antibody-dependent cell mediated cytotoxicity (ADCC) via better affinity to FcγRIII.

The specification discloses mutations at various positions in Fc region of anti-IgE antibody influence its binding affinity to Fcγ receptors (see Table 6-9). The specification further discloses that single alanine mutation in various position in Fc region changes the affinity of anti-HER2 IgG1 to FcγRIIIA; and the variants with better affinity to FcγRIIIA show greater ADCC activity towards breast tumor cells in the presence of effector cells isolated from normal human volunteers (see Figure 20 and page 73, lines 1-5). Furthermore, the instant specification asserts that in vivo uses of the polypeptide variants for treating patient (see page 58, lines 24-30).

The instant specification only provides in vitro assays using antibodies to determine whether a particular variant is effective in ADCC. It is not clear that reliance on the in vitro evidence of enhanced ADCC or even animal models accurately reflects the clinical efficacy of the antibody variants. In fact the state of the art (Eccles, Breast Cancer Res. 2001, 3:86-90) recognizes that there is no formal prove the ADCC operates in patients and some monoclonal Abs that perform well in ADCC assays fail in clinical trials (see page 88, lines 5-16 of the 2nd paragraph on the right column). Further, Eccles et al teach that specificity of binding of Ig isotypes to different FcR isoforms is complex with both CH2 regions and CH2/CH3 interface being implicated (see page 89, lines 12-15 of the left column). Similarly, Tutt et al (The Journal of Immunology, 1998, 161:3176-3185) show that in monoclonal antibody therapy of B cell lymphoma, the signaling activity on tumor cells appears more important than the recruitment of effectors (seeTitle, in particular). Tutt et al describe that antibodies shown binding and cytotoxic activity against mouse B cell tumor in vitro do not seem to be effective in vivo (see page 3180, lines 16-18 of the right column).

Therefore, in view of lack of working examples, the scope of claims drawn to any polypeptide comprising an Fc region, guidance for treating a disorder in a patient using the polypeptide variants, the stat of art teachings, undue experimentation would be required to practice the claimed methods with reasonable expectation of success.

Furthermore, the specification does not reasonably provide enablement for method of treating any disorders by administering variants of any polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention. A person skill in the art is not enabled to make and use variants of any parent polypeptides as encompassed by the full breadth of the claims as currently recited to treat any disorders. The term "polypeptide" as recited encompasses any proteins. It is well known in the art at the time the invention was made that ADCC is a process where the Fc R of the natural killer cells and other leukocytes bind to antibody-coated cells targets and destroy them (see page 3, 2nd paragraph of the instant specification). The antibodies mediating ADCC must have Fc region (for binding of Fc R) as well as regions for binding of target cells. Thus the structure of polypeptide cannot be readily envisioned by one skilled in the art based upon the guidance provided in the specification. Moreover, an enhanced ADCC would only be beneficial to disorders that have unwanted target cells (e.g. tumor cells). Therefore, applicant does not appear to provide a sufficiently enabling disclosure regarding how to make and use variants of any polypeptides other than antibodies, for the method of treating any disorders. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

The term "polypeptide" only have the notion that the protein has amino acid residues; there is insufficient biochemical or structural information to enable the skilled artisan to make and use the variants of any "parent polypeptide" as broadly claimed for the method of treating any disorders. The experimentation left to those skilled in the art is unnecessarily and improperly, extensive and undue.

5. Claims 1, 5-11, and 14 are rejected under USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following *written description* rejection is set for the herein.

There is insufficient description in the specification as filed of variant of "parent polypeptide" as recited in the instant claims. Only antibodies appear to have clear written support in the specification as filed. Therefore, the term "variant of parent polypeptide" does not meet the written description provision of 35 USC 112,first paragraph.

The specification as filed does not appear to provide adequate wriitten description support for "variant of polypeptide", other than antibodies. The term "polypeptide" encompasses any proteins that have amino acids. However, as noted supra, only antibodies that can bind target cells and have Fc region can mediate ADCC. Thus, the structure of any polypeptide cannot be readily envisioned by one skilled in the art based upon the guidance provided in the specification as field. Consequently, the conception in variant of parent polypeptide mediating ADCC cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the polypeptide. Adequate written description requires more than a mere statement that it is part of he invention.

Therefore, only variants of parent antibodies, but not the full breadth of the claims of variant of parent polypeptide meet the written description provision of 35 USC 112, first paragraph.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 USC 112 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
September 22, 2005

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
9/20/05